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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/921,645	08/03/2001	Thomas J. Meade	A-64411-2/RFT/RMS/RMK	6483

7590 11/17/2003

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EXAMINER

STRZELECKA, TERESA E

ART UNIT

PAPER NUMBER

1637

DATE MAILED: 11/17/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

File A-64411-2 Atty RMS/RMK/SL
Due Date 2/17/04
Type 3mth resp Refs Isr

Office Action Summary

Application No.

09/921,645

Applicant(s)

MEADE ET AL.

Examiner

Teresa E Strzelecka

Art Unit

1637

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 14 July 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 51-69, 71, 72 and 74-93 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 51-69, 71, 72 and 74-93 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 13) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.
a) ☐ The translation of the foreign language provisional application has been received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 14072003. 6) ☐ Other:

DETAILED ACTION

1. This office action is in response to an amendment filed on July 14, 2003. Claims 51-79 were pending. Applicants amended claims 51-69, 71, 72 and 74-79 and added new claims 80-93. Formerly present claims 70 (73 before renumbering) and 73 (76 before renumbering) have been omitted from the currently pending set of claims. It is not clear whether the claim has been cancelled or inadvertently omitted.
2. Applicant's amendments and arguments obviated the following rejections: rejection of claims 51, 59, 60, 61, 63, 64, 74 and 75-78 under 35 U.S.C 112, second paragraph. Rejection of claims 51-58, 60-61, 64-74 and 79 under 35 U.S.C 102(e) over Wohlstadter et al. are maintained for reasons given in the Response to Arguments section.
3. Applicants' amendments obviated objection to the specification and claims 51, 62, 67 and 68.
4. The terminal disclaimer filed on July 14, 2003 disclaiming the terminal portion of any patent granted on this application which would extend beyond the expiration date of U.S. Patents No. 6,265,155 B1 and 6,291,188 B1 has been reviewed and is accepted. The terminal disclaimer has been recorded.
5. Claims 51-69, 71, 72 and 74-93 are pending and will be examined.
6. This office action is made non-final because of new grounds for rejection for claims 59, 63 and 75-78.

Information Disclosure Statement

7. The information disclosure statement (IDS) submitted on July 14, 2003 was filed after the mailing date of the first office action on January 3, 2003. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered

Art Unit: 1637

by the examiner. References A0, A5, A11, A17, A19, A25, A26, A29, A41, A42 were not considered, since they were duplicates of previously considered references. Reference C10 was not considered since it was not provided.

Response to Arguments

8. Applicant's arguments filed July 14, 2003 have been fully considered but they are not persuasive.

A) Applicants argue that the instant application is entitled to a priority date of the application No. 08/475,051, now U.S. Patent No. 5,824,473, since the priority was claimed to a "continuing application", which includes continuation-in-part application, for which the disclosure does not need to be identical (response, page 8, last paragraph, continued on page 9). However, according to rule 37 C.F.R. 1.78 (a) (2) (i),

Except for a continued prosecution application filed under § 1.53(d), any nonprovisional application claiming the benefit of one or more prior-filed copending nonprovisional applications or international applications designating the United States of America must contain or be amended to contain a reference to each such prior-filed application, identifying it by application number (consisting of the series code and serial number) or international application number and international filing date and indicating the relationship of the applications. Cross references to other related applications may be made when appropriate (see § 1.14).

Therefore, Applicants did not correctly identify the relationship between the instant application and the priority applications. In addition, the above application does not contain support for the claims of the instant application. In particular, no support is provided for an array on a solid support, the array comprising regions comprising an electrode and self-assembled mixed monolayer, or for using such an array to detect target nucleic acids. Therefore, the priority date of the instant claims is February 28, 1997, as stated in the previous office action.

B) With respect to art rejections, Applicants argue that Wohlstadter et al. do not anticipate claims 51-58, 60-61, 64-74 and 79, since the instant invention teaches a 3-component system, whereas Wohlstadter et al. teaches a 4-component system, therefore Wohlstadter et al. do not expressly and inherently disclose each and every element of the instant invention (Response, page 11, the last paragraph and page 12, paragraphs 1 and 2). This argument is found not persuasive, since Wohlstadter et al. expressly teach a 3-component system consisting of a self-assembled monolayer, a linker and a probe nucleic acid (col. 56, lines 14-40). Furthermore, the claim contains a limitation "mixed monolayer comprising", therefore claim language does not exclude system with more than three components. In addition, Applicants' system also contains blocking moieties, which may form a fourth component. Since the binding of linker to the nucleic acid is covalent (col. 56, lines 38, 39), Wohlstadter et al. anticipates the above-mentioned claims.

Claim Rejections - 35 USC § 112

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claims 71 and 72 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A) Claim 71 is indefinite because it depends from claim 70, which is not present in the currently pending set of claims.

B) Claim 72 recites the limitation " $n \geq 6$ " in line 1/2. There is insufficient antecedent basis for this limitation in the claim. Claim 72 depends from claim 51, which does not contain a limitation related to n .

Double Patenting

11. Claim 89 is objected to under 37 CFR 1.75 as being a substantial duplicate of claim 88.

When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

12. Applicant is advised that should claim 88 be found allowable, claim 89 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Claim interpretation

13. Before proceeding with the rejection, definitions of terms "electrode" and "shielding" will be provided. Applicants do not define the term "electrode" in the specification. However, Applicants define "solid support comprising a metallic surface":

"... By "solid support comprising a metallic surface" or grammatical equivalents herein is meant a surface that has a metallic layer. Suitable metallic layers include any metals to which thiol groups may be attached, with gold and copper being preferred, and gold being particularly preferred. Thus, any material which can be made to contain a metallic layer or film can be used as a solid support. Accordingly, the entire surface may be metal, or only a thin layer or film of metal on the top of a different material may be used. Thus, for example, glass, plastic, polymers, graphite, or metals other than gold and copper can be used as a support, with at least a portion of one side of the support having a metallic surface."

Art Unit: 1637

Therefore, the term "electrode" will be considered as meaning "a solid support comprising a metallic surface".

14. The term "shielding" is used here in its everyday meaning, i.e. "preventing physical contact". Therefore, "blocking moieties shielding nucleic acids from the electrode" means any structural elements which prevent contact of target and/or probe nucleic acids with the electrode.

Claim Rejections - 35 USC § 102

15. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

16. Claims 51-58, 60-62, 64-73, 79, 80, 82, 83, 85-89 and 93 are rejected under 35 U.S.C. 102(e) as being anticipated by Wohlstadter et al. (U.S. Patent No. 6,066,448 A; cited in the previous office action).

Art Unit: 1637

Regarding claims 51 and 80, Wohlstadter et al. teach a method for detecting nucleic acid hybridization, the method comprising:

a) adding a target nucleic acid to an array to form at least a first hybridization complex, said array comprising a solid support having a plurality of regions, each region comprising an electrode and a self-assembled mixed monolayer (Wohlstadter et al. teach hybridization of an analyte nucleic acid (=target nucleic acid) to nucleic acid probes linked to a PMAMS (patterned, multi-array, multi-specific) surface, (col. 54, lines 38-53). The PMAMS, comprising an array of binding domains (= a plurality of regions), are prepared on a solid support by patterning of self-assembled monolayers. Mixed monolayers may be used to control the density of binding reagents (col. 36, lines 16-20). Binding domains contain binding reagents, such as nucleic acids (col. 11, lines 13-24, 40-50; col. 20, lines 30-67). A plurality of binding domains with different nucleic acid probes in each of them can be prepared (col. 45, lines 56-65). The support may be metal (col. 12, lines 5-9).)

comprising

i) blocking moieties, having a first end attached to said electrode, wherein said blocking moieties shield nucleic acids from said electrode (Wohlstadter et al. teach blocking molecules and blocking polymers covalently attached to the surface (col. 33, lines 63-65; Fig. 28). Therefore, as can be seen from Fig. 28, the blocking molecules will prevent contact of any other molecule, such as a nucleic acid, with the surface. In an alternative interpretation, since the linker to which the nucleic acid is attached prevents contact of the nucleic acid with the electrode, the linker itself can be considered as a blocking moiety. Also, there are linkers in the monolayer without other molecules attached to them, and these serve as blocking molecules as well.);

and

ii) at least one modified nucleic acid comprising a nucleic acid and a linker moiety having a first and second end;

wherein said first end of said linker is attached to said electrode and said second end is covalently attached to said nucleic acid (Wohlstadter et al. teach attachment of OH-terminated alkane thiol, $\text{SH}-(\text{CH}_2)_{11}-\text{OH}$ (= linker moiety) to a gold surface, followed by addition of nucleic acids to form modified nucleic acids (col. 56, lines 14-40), which can be attached to the linker covalently (col. 56, lines 38, 39).);

wherein at least two different regions comprise different probe nucleic acids (Wohlstadter et al. teach a plurality of binding domains with different nucleic acid probes in each of them (col. 45, lines 56-65).);

b) adding an agent that distinguishes between single and double stranded nucleic acids (Wohlstadter et al. teach using electrochemical labels which distinguish between single-stranded and double-stranded DNA, such as intercalators (col. 35, lines 13-28).); and

c) detecting the presence of said first hybridization complex (Wohlstadter et al. teach detection of double-stranded oligonucleotides using electrochemical labels which distinguish between single-stranded and double-stranded DNA, such as intercalators (col. 35, lines 13-28).).

Regarding claims 52, 53 and 82, Wohlstadter et al. teach attachment of binding reagents to the surface using a sulfur linkage (alkane thiol) (col. 17, lines 62-67; col. 56, lines 14-40).

Regarding claim 54, Wohlstadter et al. teach gold electrodes (col. 27, lines 21-25).

Regarding claims 55, 57 and 83, Wohlstadter et al. teach a linker (spacer) with a formula $\text{SH}-((\text{CH}_2))_n-\text{X}$ (thiol alkane), which binds to a gold surface. The spacer is linked to a linking group, which is in turn linked to a binding reagent (col. 52, lines 55-60; col. 53, lines 1-51; col. 56, lines 23-36). Blocking molecules and blocking polymers are covalently attached to the surface via

linker molecules (col. 33, lines 56-64; Fig. 28). Therefore, since the blocking moieties are attached to the linkers containing alkyl groups, they comprise alkyl groups, anticipating the limitation of claim 57. Also, (see the explanation for claim 51), since the linker itself can be considered as a blocking moiety, the claim limitation is anticipated.

Regarding claims 56 and 71, Wohlstadter et al. teach a linker (spacer) with a formula $\text{SH}-((\text{CH}_2))_n\text{-Y}$ (thiol alkane), where R1 and R2 are hydrogen (col. 52, lines 55-60; col. 53, lines 1-51; col. 56, lines 23-36).

Regarding claims 58, 72 and 87, Wohlstadter et al. teach that the alkane thiols contain from 1 to 100, 2 to 24 or 2 to 18 carbons (col. 35, lines 65-67; col. 36, lines 1-3), anticipating the limitation of n greater than 6.

Regarding claim 60, Wohlstadter et al. teach a linker (spacer) with a formula $\text{SH}-((\text{CH}_2))_n\text{-X}$ (thiol alkane) (col. 52, lines 55-60; col. 53, lines 1-51; col. 56, lines 23-36). Since the linker itself can be considered as a blocking moiety, and it is a straight chain alkyl group, the claim limitation is anticipated (see the explanation for claim 51).

Regarding claims 61 and 68, Wohlstadter et al. teach that the alkane thiols contain from 1 to 100, 2 to 24 or 2 to 18 carbons (col. 35, lines 65-67; col. 36, lines 1-3), anticipating the limitation of alkyl ranging from 1 to 20 carbon atoms.

Regarding claims 62 and 85, Wohlstadter et al. teach a plurality of different blocking moieties, such as polymers or proteins (col. 32, lines 6-10; col. 33, lines 63-65).

Regarding claim 64, Wohlstadter et al. teach a linker (spacer) with a formula $\text{SH}-((\text{CH}_2))_n\text{-X}$ (thiol alkane) (col. 52, lines 55-60; col. 53, lines 1-51; col. 56, lines 23-36). Since the linker itself can be considered as a blocking moiety, and it is an alkyl group, the claim limitation is anticipated (see the explanation for claim 51).

Regarding claim 65, Wohlstadter et al. teach a linker (spacer) with a formula $\text{SH}-((\text{CH}_2))_n-\text{X}$ (thiol alkane) (col. 52, lines 55-60; col. 53, lines 1-51; col. 56, lines 23-36), where the alkane thiols contain from 1 to 100, 2 to 24 or 2 to 18 carbons (col. 35, lines 65-67; col. 36, lines 1-3), anticipating the limitation of $n = 16$. Since the linker itself can be considered as a blocking moiety, the claim limitation is anticipated (see the explanation for claim 51).

Regarding claim 67, Wohlstadter et al. teach a linker (spacer) with a formula $\text{SH}-((\text{CH}_2))_n-\text{X}$ (thiol alkane) (col. 52, lines 55-60; col. 53, lines 1-51; col. 56, lines 23-36), therefore Wohlstadter et al. teach a straight chain alkyl group.

Regarding claims 69 and 86, Wohlstadter et al. teach a linker (spacer) with a formula $\text{SH}-((\text{CH}_2))_n-\text{X}$ (thiol alkane) (col. 52, lines 55-60; col. 53, lines 1-51; col. 56, lines 23-36), where the alkane thiols contain from 1 to 100, 2 to 24 or 2 to 18 carbons (col. 35, lines 65-67; col. 36, lines 1-3), anticipating the limitation of $n = 16$.

Regarding claims 74, 88 and 89, Wohlstadter et al. teach blocking moieties comprising phosphate (= phosphorus containing moiety) (col. 32, line 11).

Regarding claims 79 and 93, Wohlstadter et al. teach intercalating agents (col. 35, lines 25-28).

Claim Rejections - 35 USC § 103

17. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

18. Claims 59, 63, 81, 84 and 85 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wohlstadter et al. and further Keyyem et al. (U.S. Patent No. 6,096,273).

Art Unit: 1637

A) Teachings of Wohlstadter et al. are discussed above. Wohlstadter et al. teach polymers as blocking moieties, but do not teach blocking moieties being branched molecules.

B) Keyyem et al. teach attachment of nucleic acids to electrodes (Abstract). Keyyem et al. teach attachment of passivation agents (= blocking molecules) in the form of monolayers to electrodes (col. 23, lines 35-65). The passivation agents include branched alkyl groups (col. 24, lines 29-35).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to have used the branched molecules of Keyyem et al. in the method of Wohlstadter et al. The motivation to do so, provided by Keyyem et al., would have been that addition of alkyl groups altered packing of the moieties on the electrode, flexibility and a degree of hydrophobicity of the oligomers (col. 24, lines 29-34), i.e. providing control over the properties of the monolayers.

19. Claims 75-78 and 90-92 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wohlstadter et al. and Keyyem et al. (U.S. Patent No. 6,096,273).

A) Teachings of Wohlstadter et al. are discussed above. Wohlstadter et al. teach attachment of nucleic acids to linkers, but do not teach attachment at a 2' position of a ribose (claims 75 and 90), at a 3' position of a ribose (claims 76 and 91), at a base (claims 77 and 92) or at a phosphate (claim 78).

B) Regarding claims 75, 76, 90 and 91, Keyyem et al. teach attachment of nucleic acid molecules to conductive oligomers (= linkers) at a 2' or 3' positions of ribose (col. 15, lines 6-11).

Regarding claims 77 and 92, Keyyem et al. teach attachment of nucleic acid molecules to conductive oligomers at a base (col. 13, lines 44-59).

Regarding claim 78, Keyyem et al. teach attachment of nucleic acid molecules to conductive oligomers at a phosphate (col. 16, lines 14-27).

It would have been *prima facie* obvious to one of ordinary skill in the art to have used the covalent attachments of nucleic acids to conductive oligomers of Keyyem et al. in the method of Wohlstadter et al. The motivation to do so, provided by Keyyem et al., would have been that attachment of nucleic acids to conductive oligomers "provides for novel gene probes, which are useful in molecular biology and diagnostic medicine. In this embodiment, single stranded nucleic acids having a predetermined sequence and covalently attached electron transfer moieties, including an electrode, are synthesized. The sequence is selected based upon a known target sequence, such that if hybridization to a complementary target sequence occurs in the region between the electron donor and the electron acceptor, electron transfer proceeds at an appreciable and detectable rate. Thus, the invention has broad general use, as a new form of labelled gene probe. In addition, since detectable electron transfer in unhybridized probes is not appreciable, the probes of the present invention allow detection of target sequences without the removal of unhybridized probe. Thus, the invention is uniquely suited to automated gene probe assays or field testing." (col. 5, lines 6-22).

20. No claims are allowed.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Teresa E Strzelecka whose telephone number is (703) 306-5877. The examiner can normally be reached on M-F (8:30-5:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached at (703) 308-1119. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Application/Control Number: 09/921,645
Art Unit: 1637

Page 13

TS
November 13, 2003

TS



JEFFREY FREDMAN
PRIMARY EXAMINER